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CD34-Negative B-Lymphoblastic Leukemia/Lymphoma Presenting as Cutenous Lesions at Infancy: A Case Report

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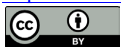
Abstract

Acute lymphoblastic leukemia/lymphoma is a highly aggressive neoplasm of precursor lymphoid (blast) cells. There are 2 main subtypes based on lymphoid lineage; B lymphoblastic leukemia/lymphoma (B-ALL/LBL) and T lymphoblastic leukemia/lymphoma (T-ALL/LBL). B-ALL/LBL commonly presents with fever, fatigue, bone or joint pain, bleeding or anorexia (signs of bone marrow infiltration), lymphadenopathy, hepatosplenomegaly, involvement of skin, soft tissue and testes, with a predilection for the central nervous system. Immature cell markers, such as CD34 and TdT, can help to differentiate lymphoblasts from Burkitt lymphoma which, is considered a mature high-grade B cell lymphoma that mimics lymphoblastic lymphoma/leukemia. Unfavorable prognostic factors include: infancy and adult age of diagnosis, high white blood cell count, slow response to initial therapy, central nervous system involvement at the time of diagnosis and Minimal residual disease after therapy. We present a case report of a 4 months old infant seen at a Tertiary Hospital with a rare presentation of CD34 Negative B-lymphoblastic leukemia/lymphoma presenting as cutaneous lesions in infancy.

1. Case Report

The infant was born a healthy baby at term and weighed 3.4 kg. At the age of 2

weeks, the infant started developing skin lesions. He was admitted twice in peripheral health facilities at 2 and 3 months of age respectively and treated for severe anemia. HIV test done then was negative.

On physical examination, the infant was wasted, in respiratory distress and had a temperature of 40˚C. The skin had generalized nodules which were indurated, non-tender and the largest measuring 2 cm in diameter. Other findings included: axillary and inguinal lymphadenopathy, the liver and the spleen were palpable 3 cm and 4 cm below the costal margin respectively.

The Investigations done included a Complete blood count which showed white blood cell count of 73×10^9 cells/L predominantly lymphocytes, the absolute lymphocyte count was 56×10^9/L. Hemoglobin level was 3.9 g/dL and platelet count was 33×10^9 cells/L. There was hypoalbuminemia (2.5 g/dL) and hypokalemia (3 mmol/L) with the other blood chemistries being normal. Bilateral pleural effusion was seen on abdominal ultrasound. Peripheral blood film and bone marrow aspirate showed 90% lymphoblasts morphologically. Flow cytometry done on the marrow aspirate showed 95% of the cells were abnormal B-cells expressing CD19+, variable CD10+, CD38+, variable HLADR+ (Population in Black), minimally CD20+, Light chain negative, and aberrant variable CD7+. A skin biopsy taken from the right forearm showed infiltration of subcutaneous tissue with sheets of small lymphoid cells with a hyperchromatic nucleus and scanty cytoplasm as shown in Figures 1-3. These features are consistent with B-cell acute lymphoblastic leukemia/lymphoma.

The child was transfused with packed red cells and started on induction chemotherapy according to ALL treatment protocol. This resulted in a marked reduction in the size of skin lesions and lymph nodes. On day 15th of induction with chemotherapy, the baby developed fevers and worsening leucopenia and thrombocytopenia. A repeat complete blood cell count showed Hemoglobin of 10 g/dL, Platelets of 10×10^9 cells/L and white blood cell count of 0.9×10^9 cells/L with an absolute neutrophil count of 0.4×10^9/L Blood cultures done were positive for hemolytic our species. He developed paralytic ileus leading to intestinal obstruction, he deteriorated and passed on a few weeks after admission.
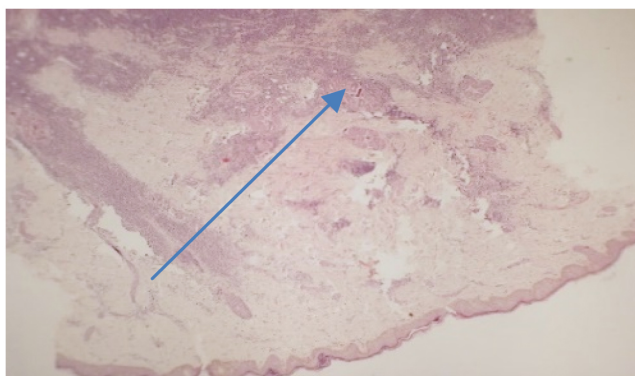
Figure 1. Skin biopsy (×4) with infiltration of subcutaneous tissue with sheets of small round blue cells (arrow).
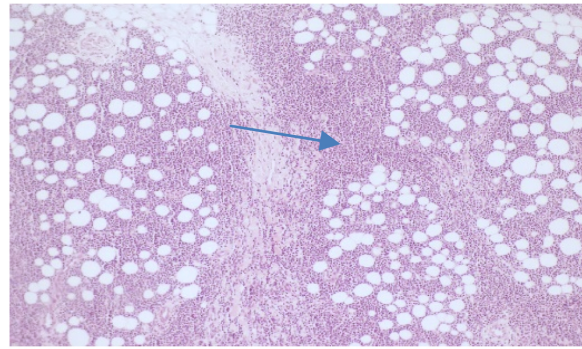
Figure 2. Skin biopsy (×10) shows infiltration of tissue with sheets of small round blue cells (blue arrow), adipocytes noted (clear white spaces).
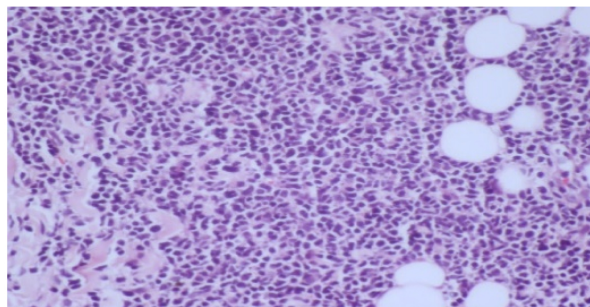
Figure 3. Skin biopsy (×40) shows infiltration of tissue with sheets of small lymphoid cells with a hyperchromatic nucleus and scanty cytoplasm.

2. Discussion

Acute Lymphoblastic Leukemia/Lymphoma is a highly aggressive neoplasm of precursor lymphoid (blast) cells. There are two main subtypes based on lymphoid lineage; B lymphoblastic leukemia/lymphoma (B-ALL/LBL) and T lymphoblastic leukemia/lymphoma (T-ALL/LBL).

B-ALL/LBL has a better prognosis in children than in adults [1] Childhood B lineage ALL/LBL has a better prognosis than childhood T lineage ALL/LBL Immature cell markers, such as CD34 and TdT, can help to differentiate lymphoblasts from Burkitt lymphoma which, is considered a mature high-grade B cell lymphoma that mimics lymphoblastic lymphoma/leukemia. Cases with tissue involvement + replacement of <25% marrow involvement by lymphoid blasts are diagnosed as lymphoblastic lymphoma (LBL). Cases with ≥25% marrow involvement is diagnosed as lymphoblastic leukemia

B-ALL/LBL commonly presents with fever, fatigue, bone or joint pain, bleeding or anorexia (signs of bone marrow infiltration) It also presents with widespread lymphadenopathy, hepatosplenomegaly, involvement of skin, soft tissue and testes and features of central nervous system involvement including convulsions, headache and cranial nerve palsies [2].

Cutaneous involvement can be an early manifestation of ALL or LBL. Cutaneous leukemic infiltrates can be observed in children with standard risk as well as in high-risk ALL. Cutaneous involvement in children with LBL is mainly as-

sociated with a B-cell precursor immunophenotype of the lymphomatous cells. The most frequent location of skin lesions in children with ALL or LBL is on the head [3].

Investigations to diagnose B-ALL/LBL include: Multimodal pathologic evaluation with some combination of morphology, flow cytometry, immunohistochemistry, cytogenetics, NGS and basic clinical laboratory tests.

Nodal excisional/Skin biopsy may be the initial diagnostic procedure for those with skin involvement, although marrow involvement is frequently present simultaneously. If marrow involvement is suspected, initial approach may consist of a complete blood count and peripheral blood smear, followed by bone marrow aspiration and biopsy. Figures 1-3 show histological sections of skin biopsy taken from the patient's forearm. The biopsy shows subcutaneous tissue infiltration with small round blue cells. Although 80% of precursor B-cell neoplasms present as acute leukemias, with bone marrow and peripheral blood involvement, a small proportion of Lymphoblastic lymphoma present with a mass lesion and have <25% blasts in the bone marrow [4].

In the peripheral blood and Bone marrow aspirates, lymphoblasts may be oval in shape and display an indented nucleus with finely dispersed chromatin and inconspicuous nucleoli as depicted in Figure 4 revised criteria to the original French American British (FAB) classification of ALL cytologic subtypes. L1 and L2 subtype segregation not shown to correlate with clinical or biologic behavior; thus, most commonly used for the descriptive purpose at this time

B-ALL/LBL express B Cell markers including CD19, CD79a, cCD22, CD22, CD24, TdT, CD34, HLA-DR, CD10 and PAX5. Pro-B-ALL expresses CD19, cytoplasmic CD79a, cytoplasmic CD22 and nuclear TdT. Common ALL express CD10 (CALLA) and late pre-B-ALL express CD20. Figure 5 shows Flow Cytometry results run on the patient's bone marrow aspirate on a 5 color, 4 tube Cytoflex platform. The results show an abnormal B-cell population (black) expressing, CD19+, variable CD10+, CD38+, variable HLADR+, minimally CD20+, Light chain negative and aberrant variable CD7+, consistent with B-ALL. Studies have shown that among B-LBL/ALL, CD34 expression was significantly
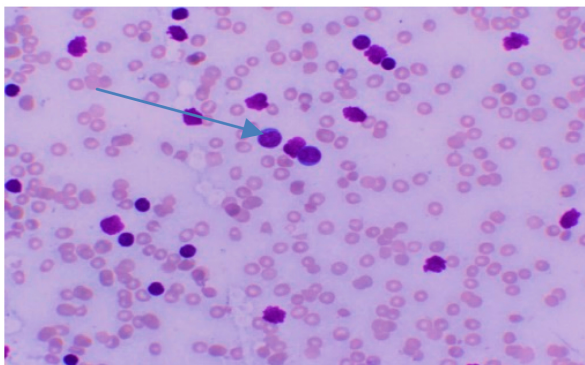
Figure 4. Peripheral blood film (×10) shows monotonous lymphoblasts with condensed chromatin and scanty cytoplasm (blue arrow).
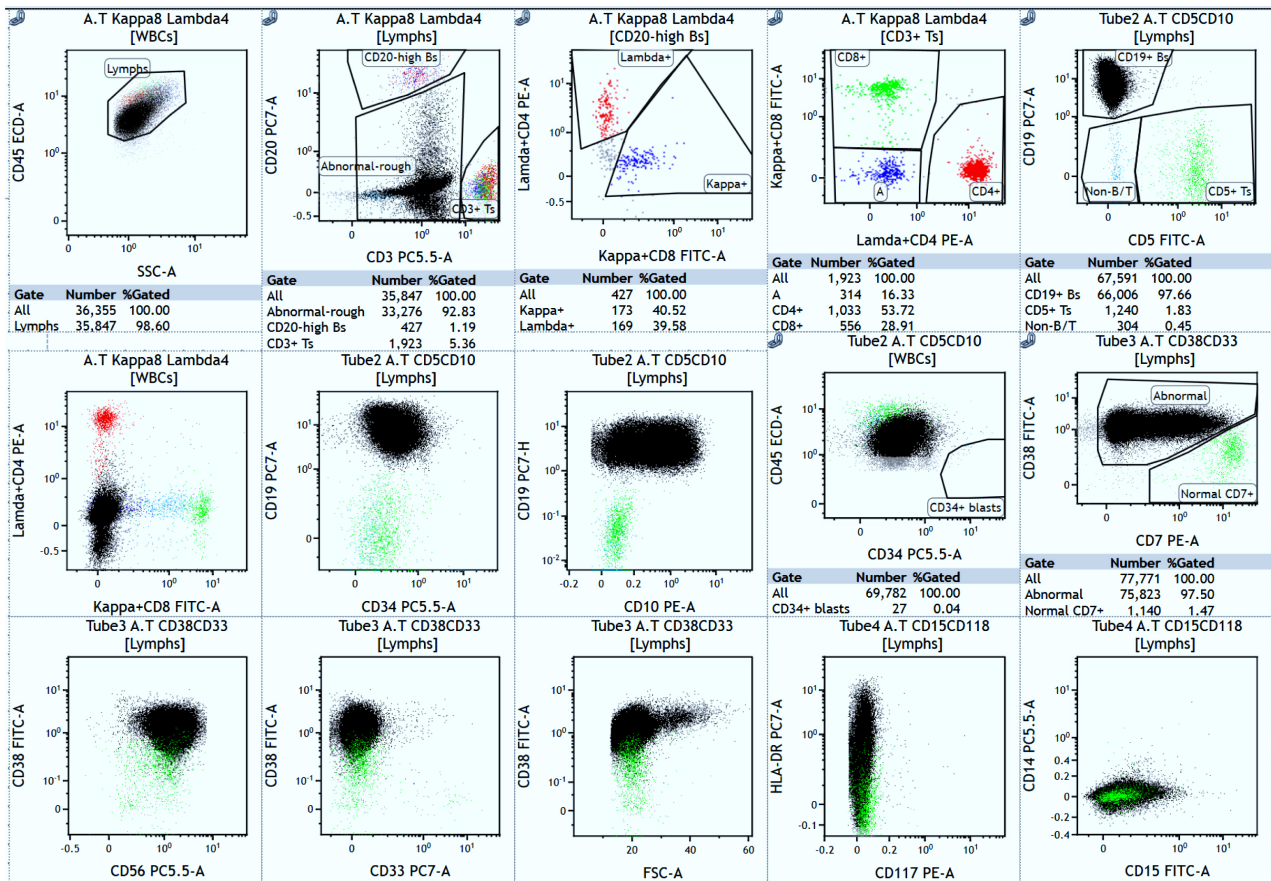
Figure 5. Flow Cytometry showed 95% of the cells are abnormal B-cells expressing CD19+, variable CD10+, dim CD38+, variable HLADR+ (Population in Black), minimally CD20+, Light chain negative, aberrant variable CD7+, Consistent with B-ALL.

associated with favorable presenting features: age 1 to 10 years, white race, absence of central nervous system (CNS) leukemia, low serum lactate dehydrogenase level, CD10 expression, and leukemic cell hyper diploidy, >50 chromosomes [5]. On the contrary, another study stated that Lack of CD34 or high CD38 expression is associated with a favorable prognosis [6]. Another study showed that TdT+/CD34+ was significantly higher in adult B-LBLs than children, which indicates blast cells are more immature in adults [7].

3. Summary

CD34 negative B-lymphoblastic leukemia is reported to be rare. Cutaneous involvement can be an early but rare manifestation of B-lymphoblastic leukemia/lymphoma. The study encompasses morphology, flow cytometry, immunohistochemistry, cytogenetics, and Molecular tests for disease characterization. Approximately 40% of AMLs and over 50% of ALLs express CD34.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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